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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,834	02/13/2002	Johannes Booij	246152015300	5546

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EXAMINER	
BERCH, MARK L	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 06/17/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,834	BOOIJ ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 7-8, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 4454069, 6417352, or 5288861.

In 4454069, see column 5, lines 36-39, which refers to Potassium clavulanate in the form of "microcrystals ... well-defined needles or waisted plates. 6417352 gives another crystallization. The form is not stated, but conditions which would be expected to obtain the rosettes were not used. In 5288861, a description of different forms appears at column 1, lines 41-45. For particle size, see column 11, lines 16-40, which discloses the distribution of particle size for conventional needles, which are of course hygroscopic. It can be seen that the average size is somewhere in the 640-1280 range for both samples A and B.

Claims 1-2, 4, 6-8, 21-22-24, 26 are rejected under 35 U.S.C. 102(b) as being anticipated by WO97/33564.

In WO97/33564, see the agglomerate at page 10, lines 13-23, and examples 7-11. Other particle size distributions appear at page 5-6. Potassium clavulanate in crystalline form may be presumed, since it is generally available in that form. With regard to claim 22, it is assumed that dependency on claim 6, not claim 5 was intended, since claim 5

does not permit anything else. With regard to claim 23, example 11 has the carrier at page 21, line 8.

Claims 1-2, 7-8, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 4863915.

In 4863915, there is taught Crystalline anhydrous amoxycillin. The sentence at column 6, lines 39-40 states that the material is hygroscopic.

Claims 1-2, 7-9, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 4584291, 3697506, 3692781, or 5250525.

In 4584291, see the product of example 12.. In 3697506, see column 6, lines 21-22. In 3692781, see column 1, lines 7-9 for the original form of cephalexin. In 5250525, see example 11. With regard to claim 9, see 4584291, lines 42-43.

Claim 1-2, 7-8, 10-13, 16, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 4138555 or 3932386 or 4073902.

In 4138555, see that Form III is crystalline and hygroscopic; note column 4, lines 54-61. The use of the solvent-antisolvent preparation is seen at column 4, lines 46-54, with dioxane as the antisolvent. In 3932386, see column 2, lines 31-34. The paragraph bridging columns 2-3 shows the crystallization procedure, with ethanol as the solvent and hexane and the antisolvent. In 4073902, see column 39, lines 25-26. The antisolvent crystallization is seen in column 39, lines 20-25.

Claim 1-2, 7-8, 10-14, 16, 21, 25 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 4659812

The β-lactam VI is taught to be "hygroscopic, crystalline ... solid" at column 12, line 24 of 4659812. The crystallization, with water as solvent and acetone as antisolvent is seen in column 12, lines 3-10. Agitation normally includes stirring.

In the above rejections, the "agglomerates" limitation is always met, because crystals are agglomerates by their very nature. With regard to claim 8, except as noted for 2 references, the references are silent on the particle size. MPEP 2112 states: "A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC" Here, the "inherent characteristic" is the particle size. Applicants would need to show that the size limitation was not met by the prior art compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 9 rejected under 35 U.S.C. 103(a) as being unpatentable over USP 4138555, 4584291, 3697506, 3692781, 3932386, 4073902, 5250525, 4659812, 4863915, 4454069, 6417352, or 5288861, or WO97/33564.

The references are discussed above. As the compounds are pharmaceuticals, it would be obvious to prepare them in sterile form, since pharmaceuticals are routinely given in sterile form. References to the use of sterile conditions appear at e.g. 4863915,

column 3, line 23 and column 4, line 13, and 5288861, column 5, line 67, which show the conventionality of such preparations.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 7-14, 16-26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The limitations "substantially free" is unclear in claim 2. Terms of degree, such as "substantial" or "relatively" are indefinite when the specification contains no "explicit guidelines" to distinguish from things which are not so, *Ex parte Oetiker*, 23 USPQ2d 1651, 1655 (1990) and *Ex parte Oetiker*, 23 USPQ2d 1641, and *Seattle Box Co. v. Industrial Crating & Packaging, Inc.* 221 USPQ 568, 574.
2. The same is true for the "high" in claim 1. How high?
3. Claim 2 is self contradictory in the phrase "non-agglomerated ... crystals" because crystals are agglomerates by their very nature.
4. Claim 19 fails to limit. This is always true. You couldn't possibly produce agglomerates in which every particle was of the same size.

5. Claim 24 fails to limit claim 21 and claim 26 fails to limit claim 22. These mean the same thing.
6. Claim 22 cannot depend on claim 5, as claim 5 requires that only Potassium clavulanate be present. Dependency on claim 6 is suggested.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is well known that clavulanic acid is an unstable, viscous oil. It cannot be crystallized; indeed, all attempts to even solidify it have failed.

Claims 10-14, 16-20, 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 10-14, 16-20, 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Potassium clavulanate, does not reasonably provide enablement for other β-lactams. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims as written say that <u>any</u> β-lactam can be made into a hygroscopic crystalline form just by stirring (claim 10) and perhaps adding a second solvent (e.g. claims 11-14). This is certainly not true. Most β-lactams are not hygroscopic to begin

with, and many precipitate from solution as amorphous powders. The fact that this procedure works with the K salt of one compound is no assurance that this will work with other compounds which bear no resemblance to Potassium clavulanate.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.

Mark L. Berch
Primary Examiner
Art Unit 1624

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June 13, 2003